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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/783,896	02/15/2001	Mark I. Greene	PENN-0743	3799

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EXAMINER
TUNG, JOYCE

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/30/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/783,896	Greene et al.
Examiner	**Art Unit**
Joyce Tung	1637

-- ***The MAILING DATE of this communication appears on the cover sheet with the correspondence address*** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Mar 21, 2003* .

2a) [ ] This action is **FINAL.** 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1, 11, 13, and 14* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1, 11, 13, and 14* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [X] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/21/2003 has been entered. Claims 1, 11 and 13-14 are pending.

Rejections and/or objected from the previous office action are hereby withdrawn. The following rejections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 11 and 13-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 5-11 of copending Application No. 09/624,946. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims 5-11 of copending Application No. 09/624,946 are drawn to a system for quantifying molecules expressing a selected epitope comprising a selected surface on which a molecule expressing a selected epitope, an epitope detector consisting of a single chain Fv or a constrained epitope specific CDR for the epitope which is modified for the attachment of an oligonucleotide and the oligonucleotide attached to the single chain Fv or the constrained epitope specific CDR. Claims 1, 11 and 13-14 of the instant Application No. 09/783,896 are drawn to a method for detecting molecules expressing a selected epitope in a sample involving immobilizing a molecule expressing a selected epitope to a selected surface, contacting the surface with an epitope detector which binds to the immobilized molecules and the epitope detector comprising an oligonucleotide attached to a monoclonal antibody, amplifying the oligonucleotide, further amplifying the amplified product with transcriptase based reaction or a replicase based reaction and then staining the amplified oligonucleotides with fluorescent dye and measuring the fluorescence emitted from the stained oligonucleotide. Since the system of the instant invention comprises the components to fulfill

the method of claims 1, 11, and 13-14 of copending Application No. 09/783,896. Therefore, these inventions are overlapping in scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. Claims 1, 11, and 13-14 are also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 09/977,716. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of copending Application No. 09/977,716 is drawn to a method for detecting molecules expressing a selected epitope in a sample involving immobilizing a molecule expressing a selected epitope to a selected surface, contacting the surface with an epitope detector which binds to the immobilized molecules and the epitope detector comprising an oligonucleotide attached to a monoclonal antibody, amplifying the oligonucleotide, staining the amplified oligonucleotides with fluorescent dye and measuring the fluorescence emitted from the stained oligonucleotide. Claims 1, 11 and 13-14 of the instant Application No. 09/783,896 are drawn to a method for detecting molecules expressing a selected epitope in a sample involving immobilizing a molecule expressing a selected epitope to a selected surface, contacting the surface with an epitope detector which binds to the immobilized molecules and the epitope detector comprising an oligonucleotide attached to a monoclonal antibody, amplifying the oligonucleotide, further amplifying the amplified product with

transcriptase based reaction or a replicase based reaction and then staining the amplified oligonucleotides with fluorescent dye and measuring the fluorescence emitted from the stained oligonucleotide. Based upon the analysis above, the methods of both application are coincident in scope.

Therefore, this is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eberwine et al. (5,922,553, issued 7/13/1999) in view of Sano et al. (5,665,539, issued 9/9/1997).

Eberwine et al. disclose a method which is for detecting a selected protein by immuno aRNA (See column, 2, lines, 37-50). The presence and quantity of labeled RNA transcript is indicative of the amount of selected protein present (See column 4, lines 33-36 and columns 7-8, claims 1-2). In the method a first antibody targeted to the selected protein is immobilized to a solid support. A RNA-promoter driven cDNA sequence is covalently coupled to a second antibody which binds the selected protein (See column 2, lines 37-51). The technique of a RNA synthesis is explicitly disclosed (See column 3, lines 9-24).

Eberwine et al. do not disclose using fluorescent dye to stain the amplified DNA.

Sano et al. disclose an immuno-PCR to detect immobilized BSA involving using the chimera-pUC19 conjugate. The chimera-pUC19 conjugate binds to the antibody which binds to the BSA. The pUC19 DNA is amplified by PCR (See column 10, lines 39 to column 11, lines 14, example 1). The products are detected by fluorescent dyes staining such as ethidium bromide and ethidium homodimer (See column 7, lines 26-32). The marker molecules are typically DNA, RNA, DNA-RNA hybrids, and the attached marker allows the amplification of its fragments by PCR with appropriate primers (See column 4, lines 3-7).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply the technique of staining the amplified DNA with ethidium bromide as taught by Sano to stain the amplified DNA produced by the immuno- aRNA synthesis of Eberwine et al. in order to quantify molecules expressing a selected epitope in a sample. The motivation is that analysis of the PCR products by agarose gel electrophoresis after staining with

ethidium bromide allows as few as 580 antigens to be detected (See column 3, lines 35-38). It would have been prima facie obvious to apply the staining technique of Sano et al. to stain the amplified DNA by the immuno- aRNA synthesis of Eberwine et al. in order to quantify molecules expressing a selected epitope in a sample

7. Claims 11 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eberwine et al. (5,922,553, issued 7/13/1999) in view of Zeytinoglu et al. (5874226, issued 2/23/1999)

The teachings of Eberwine et al. are set forth in section 6 above.

Eberwine et al. further disclose quantifying the amplified oligonucleotide detected (See column 7, claim 1) and that the selected surface to which the molecule expressing a selected epitope in a sample is immobilized is a chip or plastic well (See column 4, lines 17-36). The method involves a transcriptase based reaction to increase sensitivity and detecting the amplified oligonucleotide (See column 2, lines 37- 58).

Eberwine et al. do not disclose there are two steps involved in the method .

Zeytinoglu et al. disclose in situ immunodetection of antigens involving polymerase chain reaction (See column 1, lines 36-54). The resulting antibody/antigen complex is detected in situ or ex situ (See column 2, lines 64-67). The bound antibody is removed from the body part and processed in ex situ (See column 3, lines 11-15). An amplified step may be or may not be employed depending on the strength of the signal (See column 5, lines 5-14). Other amplification technologies are applicable, including two steps (See column 5, lines 14-16).

It would have been prima facie obvious to an ordinary skill in the art at the time of the instant invention to modify the method of Eberwine et al. by adding an additional step as suggested by Zeytinoglu et al.. The motivated is that the Zeytinoglu et al. disclose that the PCR amplification method shown is especially advantageous where the amount of antigen to be detected is very small, e.g., 500 molecules. Thus, an ordinary skill in the art would have added an additional step of amplification to obtain the enough amount of signal for detection or quantification.

Summary

8. No claims are allowable.

CONCLUSION

9. Claims 1, 11 and 13-14 is/are rejected and/or objected to for the reason(s) set forth above.

10. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

JT

May 22, 2003

ETHAN WHISENANT
PRIMARY EXAMINER